

Remarks

The undersigned confirms that a species election was required by telephone among claims 4, 6 and 7 and that the species of claim 4 was elected. However claim 4 is canceled and claim 40 is amended to include the limitations of claim 4. Claim 7 is amended herewith to indicate that the particles are those referred to in amended claim 40 and it is requested that it be restored to consideration in view of the amendments to claim 7 and claim 40.

The specification is objected to in paragraph 3 of the rejection on the basis that "erythropoietin" is misspelled therein. The only place the undersigned finds recitation of erythropoietin in the specification is at page 8 and it is spelled correctly there.

In paragraph 4 of the office action claims 12 and 34 are objected to for the same misspelling. Claims 12 and 34 are canceled to reduce potential issues.

Claims 2, 7, 9, 10, 11, 14, 18, 20, 24, 25, 26, 28, 29, 30, 32, 33, 40, 41, 42, 43, 44, 45 and 46 are in the case.

Claim 40 is amended to include the limitations of canceled claim 4 and to bring out clearly that the amount of water used is controlled to provide a particle size distribution such that from about 80% to about 98% of the particles have a diameter from about 800 to about 1500 μm . Support for this amendment can be found in the original specification (see, for example, page

10, lines 19/21 and PCT Claim 4). This amendment has the advantage of bringing the wording of the US claims more into line with the claims allowed in other jurisdictions where substantive examination of the invention has taken place. Claims 32 and 33 are amended to "a sugar" and "a cellulose" for consistency with claims 24 and 28.

Claims 42-46 are new claims, of which new Claims 42 to 44 are each dependent directly from new Claim 40, and new Claims 45 and 46 are further independent claims.

New Claim 42 defines embodiments wherein the rheology modifying agent is selected from the group consisting of starch, hydroxypropylmethylcellulose, crospovidone, sodium starch glycolate and croscarmellose sodium. Support for these embodiments can be found in the original specification (see, for example, see page 9, lines 16/21).

New Claims 43 and 44 define embodiments wherein the active component is paracetamol (or a salt or derivative thereof). We note that such embodiments are exemplified (see, for example, Example 8) but have not been heretofore claimed individually.

New claim 45 defines the process of amended Claim 40 in which the amount of water used is controlled so as to provide a particle size distribution such that about 90% to about 98% of the particles have the required diameter. Support for this process may be found in the original specification (see, for example, page 4, lines 31/34).

New Claim 46 defines the process of amended Claim 40 in which the amount of water used is controlled so as to provide a particle size distribution such that about 95% to about 98% of the particles have the required diameter. Support for these embodiments may be found in the original specification (see, for example, PCT Claim 5).

We turn now to the prior art rejections.

Claim 8-10, 14, 18, 20-24, 26, 28-30, 32, 40 and 41 are rejected under 35 U.S.C. 102 (a) as being anticipated by Speirs (U.S. 5,834,021) and claims 8-10, 14, 18, 20, 24, 26, 28-30, 32-34 and 40 are rejected under 35 U.S.C. 102 (a) as being anticipated by Patel (U.S. 2003/0180352 A1).
Reconsideration is requested.

The Office Action has not raised an objection to the novelty of the invention as defined in Claim 4 and at paragraph 24, acknowledges that at least Speirs does not specify producing a particle size distribution such that about 80% to about 98% of dried pellets having a diameter from about 800 to about 1500 μm .

Amended Claim 40 requires that the amount of water used in the process is controlled to ensure that from about 80 % to about 98 % of particles produced by the process have a diameter from about 800 to about 1500 μm . As mentioned above, the office action acknowledges (see paragraph 24) that such a process is novel over Speirs.

Patel *et al* does not disclose an extrusion/spheronization process for producing pellets having *any* particular size distribution, let alone the specific size distribution defined in amended Claim 40. In fact, Patel *et al* only exemplifies coating non-pareil seeds or producing pellets using a spray congealing process. Since there is no disclosure in Patel *et al* of an extrusion/spheronization process producing pellets having the specific size distribution defined in amended Claim 40, the process defined by this claim is novel over Patel *et al*.

On the basis that the remaining claims are all dependent, either directly or indirectly, from amended Claim 40, the embodiments of the present process defined by these claims are also novel over both Speirs and Patel *et al*.

Claims 2, 4 and 36 are rejected under 35 U.S.C. 103 (a) as being unpatentable over Speirs (U.S. 5,834,021) in view of Patel *et al* (U.S. 2003/0180352 A1) and Wolozin (U.S. 6,472,421 B1). Amended claim 40 replaces claim 4 which is canceled. Claim 36 is canceled. The office action (paragraph 25) takes the position that the invention as defined in claim 4 is obvious. However, it is our view that the office action is mistaken and has based its position on a baseless assumption regarding the teaching of Speirs. Reconsideration is requested.

In paragraph 25, the office action states that “...*Speirs does not specify from about 80 % to about 98 % of dried pellets having a diameter from about 800 to about*

1500 μm , but specifies the pellets having a diameter in the range of 1000-1400 μm ...". However, the office action has failed to indicate that Speirs actually teaches producing pellets having a diameter within a broader range, of which only an unknown portion have a diameter in the range the office action specifies.

✕ In this connection, the pellets produced directly from the process according to Example 1 of Speirs actually have diameters ranging from 700 to 1700 μm . Speirs discloses (see column 4, line 66/67) that the "...composition of the invention will usually be in the form of pellets having a diameter in the range of 700-1700 μm ...". In addition, the rate of dissolution of the various pellets produced by the process disclosed in Speirs was tested and the results depicted in the graphs of Figures 1 to 9. In each case, the pellets have diameters within the broad range from 700 to 1700 μm (see, for example, column 2, lines 35, 40, 44, 48, 52, 57, 64 and 67; column 3, lines 5, 12 and 38/40).

A portion or fraction of the total number of pellets produced by the process in Speirs will certainly have diameters ranging from 1000 to 1400 μm . However, Speirs is entirely silent about the size of the portion or fraction of the total number of pellets produced which having diameters ranging from 1000 to 1400 μm (or, indeed, from 800 to 1500 μm which is, of course, the range defined in Claim 40).

The process according to Speirs also produces significant numbers of pellets having diameters outside 1000 to 1400 μm , i.e. pellets having diameters from 700 to 1000 μm (i.e. "undersized" pellets) or from 1400 to 1700 μm (i.e. "oversized"

pellets). Again, Speirs is entirely silent about the size of the portion or fraction of the total number of pellets produced which have diameters outside the range of 1000 to 1400 μm (or, indeed, outside the range of 800 to 1500 μm according to the present invention).

In order to obtain a fraction of the total number of pellets produced in Speirs having a diameter from 800 to 1500 μm , it would be necessary to selectively "screen" all of the pellets that are produced in the process. Indeed, it is only by selectively screening the pellets produced in Speirs that the fraction of the pellets having a diameter from 1000 to 1400 μm may be obtained. The number of pellets produced by the process in Speirs that have diameters outside the required range is significant and, therefore, the process accordingly to Speirs results in a large amount of wasted pellets.

The office action may have been confused by the reference in Example 1 of Speirs to providing "...*pellets having a diameter in the range of 1000-1400 μm ...*" (see column 38/39). This reference, however, provides no information that could be considered to quantify the number or portion of pellets having the specified diameter. In contrast, all that the skilled person is able to conclude from this reference is that *some* of the pellets produced by the process have the specified diameter.

With the foregoing comments in mind, Speirs actually teaches the production of pellets having a broad range (from 700 to 1700 μm) of diameters. However, Speirs does not provide any information as regards the particle size *distribution* within that broad range. In this connection, the office action has assumed that the average particle

size in Speirs is within 1000 to 1400 μm . However, this assumption is based on a further assumption that there is a particular distribution of particle sizes within the broad range. However, there is no basis in Speirs to make this further assumption.

In contrast, it is possible that the majority of pellets produced in Speirs have diameters towards either the upper or lower limits of the broad range, resulting in an average particle size outside the range of 1000 to 1400 μm . In fact, based on the information provided in Speirs, it is impossible to determine whether or not the average diameter of the particles produced in Speirs is within the narrower range of 1000 to 1400 μm as assumed by the office action.

Speirs teaches (see column 4, line 66 to column 5, line 1) that the composition of the invention will usually be in the form of pellets having a diameter in the range of 700-1700 μm , preferably 1000-1400 μm . However, Speirs does not explain why the fraction of particles having a diameter from 1000-1400 μm would be preferred over particles outside this range.

The office action would appear to have assumed that the selection of 1000 to 1400 is because most of the pellets are within this range. However, it is by no means inevitable that the preference for the narrower range is merely because of the number of pellets in this range. In contrast, this explanation is only one of a number of possible explanations for this preference. For example, the preference could be because these pellets having a diameter from 1000 to 1400 μm are particularly suitable to provide the required drug release profile in the intestine. In addition, as explained in the introduction of the present application, the preference could be

because such pellets may be coated most efficiently and/or may allow the optimum number of pellets to be encapsulated. The point is that the skilled person would appreciate that these other explanations are irrespective of the actual number of pellets within this range and it is by no means inevitable that there is an overlap in the ranges of particles sizes as suggested by the office action.

The present inventor has discovered that it is possible to produce pellets having an extremely narrow particle size distribution (up to 95% to 98% having a diameter from 800 to 1500 μm) in an extrusion/spheronisation process by carefully controlling the amount of water used in the process. In this way, it is possible to avoid producing significant quantities of pellets outside the desired range which have to be screened out and discarded (as in Speirs).

It is acknowledged that the skilled person would be aware that particle size and particle size distribution in such pellet manufacturing processes can be varied by changing any of a number of aspects and parameters of the process. For example, Patel *et al* discloses (see paragraph [0322]) that “...*the size and size distribution of pellets...can be adjusted by one skilled in the art by the inclusion of additives, choice of equipment, and processing conditions*”. However, what was not known before the priority date of the present invention is that carefully controlling the amount of water used in the process could achieve such a high degree of control over the particle size distribution.

Whilst it may be true that the skilled person could, by trial and error, determine the amount of water used in the process exemplified in Speirs, such an amount of water would only be sufficient to produce pellets having a broad size distribution, i.e. diameters from 700 to 1700 μm . There is nothing in Speirs to suggest that, by carefully *controlling* the amount of water, it is possible to obtain a narrow particle size distribution such that from 80 to 98% of the particles produced by the process have a diameter from 800 to 1500 μm . In fact, Speirs does not provide any indication at all that pellets having a narrower size distribution could be produced directly from the process. Thus, the skilled person has no idea from Speirs that pellet size distribution could be controlled by carefully controlling the amount of water used (or by any other means for that matter). On this basis, the present invention as defined in amended Claim 40 has an inventive step over Speirs when considered alone.

Neither Patel *et al* nor Wolozin discloses that particle size distribution in a pelletization process may be controlled to any extent, let alone to the extent claimed in the present invention, by carefully controlling the amount of water used in the process. In fact, we note that Patel *et al* only mentions “water” in a handful of occasions and even then only in the context of water-soluble compounds (see para [0104]) or as an additive in the composition itself (see para [0255]) and not as a solvent for a pelletization process. Moreover, Wolozin does not disclose a pelletization process at all, let alone the use of water in such a process. Therefore, even if the skilled person were to combine the teachings of Speirs with either of these references, he would not arrive at a process falling within the scope of amended

Serial Number: 10/581,595
Attorney Docket: SPEI3003/ESS

Claim 40. On this basis, the process of amended Claim 40 has an inventive step over Speirs when taken in combination with either Patel *et al* or Wolozin.

The remaining new claims are either dependent from amended Claim 40 or are independent claims defining an even narrower particle size distribution (new Claims 45 and 46. Thus, the subject matter of the remaining claims also has an inventive step over Speirs when considered alone or in combination with either Patel *et al* or Wolozin.

In view of the above the obviousness rejection is defective.

It is noted that claim 25 is not subjected to detailed rejection but is only rejected on the office action summary page.

Allowance is requested.

Respectfully submitted,
BACON & THOMAS, PLLC

By: 

Eric S. Spector
Registration No. 22,495

BACON & THOMAS, PLLC
Customer 23364
625 Slaters Lane - 4th Floor
Alexandria, VA 22314-1176
Telephone: (703) 683-0500
Facsimile: (703) 683-1080

Date: December 17, 2009